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EXAMINER	
KIM, YOUNG J	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,581	HANNA, MICHELLE M.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-84,106-111,113,114 and 130-148* is/are pending in the application.

4a) Of the above claim(s) *72-84,106-111,136,137 and 141* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-71,113,114,130-135,138-140 and 142-148* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present Office Action is responsive to the Amendment received on June 11, 2008.

Preliminary Remark

Claims 1-54, 85-105, 112, and 115-129 are canceled.

Claims 72-84, 106-111, 136, 137, and 141 remain withdrawn as being drawn to non-elected invention, non-election which was made with traverse.

Information Disclosure Statement

The IDS received on June 11, 2008 is acknowledged.

Applicants' remark regarding the reference NPL23 therein, has been noted and duly considered.

Claim Objections

The objection to claim 133 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, made in the Office Action mailed on December 11, 2007 is withdrawn in view of the Amendment received on June 11, 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 55-70, 113, 130, 133-135, 138-140, 142-148 under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (U.S. Patent No. 5,215,899, issued June 1, 1993) in view of Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference), made in the Office Action mailed on December 11, 2007 is maintained for the reasons already of record.

Applicants' arguments presented in the Amendment received on June 11, 2008 have been carefully considered but they are not found persuasive for the reasons set forth in the, "Response to Arguments" section.

The Rejection:

Dattagupta discloses a method of detecting a target nucleic acid in a sample, wherein said method comprises:

a) hybridizing a single-stranded target polynucleotide with an abortive promoter cassette (Figure 4, hairpin probe is hybridized with a nucleic acid target);

b) incubating said target polynucleotide with an RNA polymerase (column 3, line 28), an initiator (column 3, line 29; Figure 4, step (II));

c) synthesizing an oligonucleotide transcript that is complementary to the initiation start site of the abortive promoter cassette, wherein the initiator is extended, producing multiple reiterative oligonucleotide transcripts;

d) and detecting the reiterative oligonucleotides (column 11, lines 26-35).

With regard to claims 69 and 133, the hairpin probe of Dattagupta is disclosed as being single, self-complementary contiguous oligonucleotide to which RNA polymerase can bind to form a transcription bubble (see Figure 4).

With regard to claims 57-60, the initiator is disclosed as being labeled (thus, modified; column 11, line 50), wherein said label is fluorophore moiety (column 11, lines 50-55).

With regard to claims 61, 62, and 146 the polymerase is disclosed as being DNA-dependent RNA polymerase (column 5, line 20) as well as RNA-dependent RNA polymerase (column 5, lines 23-24) and RNA polymerases derived from bacteriophages (column 5, lines 26-27).

With regard to claim 63, the reiterative transcripts are of desired, specific size (column 12, lines 18-19).

With regard to claims 64, 68, and 135, the initiator is a nucleotide (column 11, line 45).

With regard to claims 66, 67, 144, and 145, the target nucleic acid DNA or RNA (column 7, lines 38-39).

With regard to claims 138-140, ribonucleotides are labeled (column 11, lines 50-51; column 9, line 39).

With regard to claim 130, Dattagupta discloses that the sample may comprise food, body fluid, urine, blood, milk, sputum, saliva, stool, lung aspirates, throat or genital swabs (column 7, lines 31-38).

Dattagupta does not disclose the incorporation of a terminator in their reaction.

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) hybridizing a single stranded target polynucleotide with an abortive promoter cassette comprising a sequence that hybridizes to the a single-stranded target polynucleotide, and a region that can be detected by transcription by a polymerase (Figure 4, see primer

comprising a sequence complementary to the target nucleic acid, and a region which is a T7 promoter or T3 promoter, which is recognized by a polymerase);

b) incubating said target polynucleotide with an RNA polymerase (with T7 or T3 RNA polymerase; see Figure 4), an initiator (or 1mM GMP; see page 3456, 2nd column, bottom paragraph) and a terminator (fluoresecent dye terminator; see page 3457, 1st column, bottom paragraph);

c) synthesizing oligonucleotide transcripts that is complementary to the initiation start site of the abortive promoter cassette, until dye terminator is incorporated in to the transcription product (see page 3457, Figure 4);

d) detecting the oligonucleotide transcripts by electrophoresis sequencing method (see Figure 5; page 3460, 1st column).

With regard to claim 134, the detection is achieved by the use of a modified nucleotide (fluorescent dye terminator; *see* page 3460, 1st column), particularly tetramethyl rhodamine (or TMR) (page 3456, Figure 2; Sasaki et al.).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dattagupta and Sasaki et al., thereby arriving at the invention as claimed for the following reasons.

Dattagupta clearly provides that multiple transcripts can be derived from their method, wherein the multiple transcripts are provided by the use of a hairpin nucleic acid construct comprising a promoter sequence. While Sasaki et al. involve a different method for transcriptional sequencing, one of ordinary skill in the art would have clearly recognized that the method provided for by Dattagupta would have also been capable of conducting transcriptional sequencing by incorporating nucleotide chain terminators in their reaction.

One of ordinary skill in the art would have had a reasonable expectation of success at combining the teachings since both methods involve the generation of nucleic acid constructs comprising promoter sequences.

In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the teachings of Dattagupta and Sasaki et al. for the purpose of detection/characterizing pathogens (such as RNA virus) in a sample, for the well known benefit of survival of mankind.

Such benefit is clearly implied by Sasaki et al., wherein the artisans explicitly state that their method would be useful in diagnostics, clinical diagnosis and genome sequencing. Clearly, one of ordinary skill in the art would have recognized that clinical diagnosis would undoubtedly include detection of pathogens in clinical samples. Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of Sasaki et al. with the teachings of Kang et al. so as to detect pathogens such as RNA-based pathogens. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at producing the combination since both teachings relied on the template nucleic acid having a promoter sequence which is recognized by the RNA dependent RNA polymerase to initiate the transcription reaction, wherein the transcription reaction is terminated by the incorporation of a terminating nucleotide.

Lastly, one of ordinary skill in the art at the time the invention was made would have recognized that any type of RNA polymerase would work equally well as Dattagupta clearly implies:

> "However, RNA probes transcribable with RNA-dependent RNA polymerases (such as in certain viruses, e.g., retrovirus and picornavirus)." (column 5, lines 23-24)

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Response to Arguments:

Applicants traverse the present rejection (page 17, bottom paragraph, Response).

Applicants disagrees with the analysis of the prior art made in the Office Action, in that the claims are not directed to transcriptional sequencing methods as discussed by Sasaki et al. (page 18, 1st paragraph, lines 1-4, Response).

This argument has been considered but is not found to be persuasive because the primary reference (Dattagupta) is drawn to a method of detection. The Sasaki reference was employed to merely demonstrate that the use of chain terminating nucleotides which are labeled was known in the art. In addition, the Sasaki reference discloses a similar method of proliferating the RNA transcripts from a target nucleic acid by use of promoter construct, which clearly would have conveyed to one of ordinary skill in the art at the time the invention was made that RNA polymerase would have been capable of incorporating chain terminating nucleotides which are labeled.

It is respectfully submitted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants' next arguments are drawn to the limitation, "abortive, reiterative process." (page 18, 1st paragraph, lines 5-9, Response).

Applicants contend that this language makes clear that the claims do not encompass embodiments wherein a plurality of transcripts of very different sizes are generated, as would be the case in transcriptional sequencing methods (Page 18, 1st paragraph, lines 7-9, Response).

This argument has been careful considered but unfortunately found to be unpersuasive.

Applicants' contention is over what is deemed to be an "abortive, reiterative process" and whether such a limitation excludes the embodiment taught by Dattagupta and Sasaki et al.

It is respectfully submitted that Applicants' own claims require that a terminator is incorporated for the transcription process to be aborted in the phrase, for example, on claim 55, step (c), "synthesizing an oligonucleotide transcript that is complementary to the initiation start site .... until said terminator is incorporated into said oligonucleotide transcript."

Clearly, Applicants' own claim does not preclude the generation of a different transcripts of differing lengths.

In addition, it is respectfully submitted that the transcripts provided for by Dattagupta in view of Sasaki et al. is deemed and abortive, reiterative process based on a reasonable broadest interpretation of the claims.

According to MPEP 2106(II)(C), claims are given their broadest reasonable interpretation:

> "Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). ***Limitations appearing in the specification but not recited in the claim are not read into the claim.*** > E-Pass Techs., Inc. v. 3Com Corp., 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily).< In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... An ***essential purpose of patent examination is to***

> ***fashion claims that are precise, clear, correct, and unambiguous***. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.").

In addition, MPEP 2106(II)(C) states that while it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not impose that limitation.

Absent a clear and explicit, not an exemplary definition in the instant specification, the transcripts provided for by the combination of the teachings of Dattagupta and Sasaki et al. are deemed to be an abortive and reiterative process. The transcripts are reiterative in that the transcripts are generated from the same template over. And said transcripts are generated by an abortive process because the transcription process is aborted prior to the second transcription process is to take place.

Nowhere in the instant specification is there found an explicit definition so as to preclude the present interpretation of the subject limitation, and therefore, it is respectfully submitted that Applicants' arguments are not found persuasive.

Next, Applicants state that Sasaki et al. do not teach hybridizing a single stranded target polynucleotide with an abortive promoter cassette (page 19, 2nd paragraph, Response).

Again, it is respectfully submitted that this aspect of the claim was taught by Dattagupta and was clearly relayed to Applicants in the previous Office Action, reiterated herein.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With regard to Applicants arguments drawn to the teachings of Sasaki et al. and Dattagupta not being capable of being combined (page 19, bottom paragraph, Response), it is respectfully submitted that said arguments are not found persuasive.

Applicants are contending that terminating dNTPs for the purpose of detection has not been employed in the art prior to the invention of the instant application. It is respectfully submitted that the use of terminal labeled dNTPs for the purpose of detection has been well known and practiced in the art (for instance WO 01/25485 A2, which conducts a single nucleotide extension for "detection" purposes. In addition, it is respectfully submitted that sequencing a target nucleic acid is broadly considered to be under the confines of "detection." The sequencing of the target nucleic acid would necessarily render to a one of ordinary skill in the art that said target nucleic acid is present (thus detected).

Lastly, with regard to Applicants' arguments regarding Dattagupta's method being too minute to be effective for sequencing (page 21, Response), it is respectfully submitted that the labeling was for the purpose of detection as relayed by Dattagupta. The use of Sasaki reference was to solely demonstrate that the use of terminators who are fluorescently labeled have been known in the art.

Therefore, the rejection is maintained for the reasons already of record.

The rejection of claims 71, 113, 114, 130, 133, 135, 138-140, and 142-148 under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (U.S. Patent No. 5,215,899, issued June 1, 1993), Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference) and Kang et al. (U.S. Patent No. 6,268,131, issued July 31, 2001), made in the Office Action mailed on December 11, 2007 is maintained for the reasons already of record.

Applicants do not make any new arguments for the present rejection in their Amendment received on June 11, 2008, but solely rely on their arguments presented for the above rejection. As the arguments have been fully rebutted as discussed above, the present rejection is maintained for the reasons already of record.

The Rejection:

Dattagupta discloses a method of detecting a target nucleic acid in a sample, wherein said method comprises:

a) hybridizing a single-stranded target polynucleotide with an abortive promoter cassette (Figure 4, hairpin probe is hybridized with a nucleic acid target);

b) incubating said target polynucleotide with an RNA polymerase (column 3, line 28), an initiator (column 3, line 29; Figure 4, step (II));

c) synthesizing an oligonucleotide transcript that is complementary to the initiation start site of the abortive promoter cassette, wherein the initiator is extended, producing multiple reiterative oligonucleotide transcripts;

d) and detecting the reiterative oligonucleotides (column 11, lines 26-35).

With regard to claim 133, the hairpin probe of Dattagupta is disclosed as being single, self-complementary contiguous oligonucleotide to which RNA polymerase can bind to form a transcription bubble (see Figure 4).

The initiator is disclosed as being labeled (thus, modified; column 11, line 50), wherein said label is fluorophore moiety (column 11, lines 50-55).

With regard to claim 146 the polymerase is disclosed as being DNA-dependent RNA polymerase (column 5, line 20) as well as RNA-dependent RNA polymerase (column 5, lines 23-24) and RNA polymerases derived from bacteriophages (column 5, lines 26-27).

The reiterative transcripts are of desired, specific size (column 12, lines 18-19).

With regard to claim 135, the initiator is a nucleotide (column 11, line 45).

With regard to claims 144, and 145, the target nucleic acid DNA or RNA (column 7, lines 38-39).

With regard to claims 138-140, ribonucleotides are labeled (column 11, lines 50-51; column 9, line 39).

With regard to claim 130, Dattagupta discloses that the sample may comprise food, body fluid, urine, blood, milk, sputum, saliva, stool, lung aspirates, throat or genital swabs (column 7, lines 31-38).

Dattagupta does not disclose the incorporation of a terminator in their reaction.

Dattagupta does not disclose that an immobilized probe be employed in their method.

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) hybridizing a single stranded target polynucleotide with an abortive promoter cassette comprising a sequence that hybridizes to the a single-stranded target polynucleotide, and a region that can be detected by transcription by a polymerase (Figure 4, see primer comprising a sequence complementary to the target nucleic acid, and a region which is a T7 promoter or T3 promoter, which is recognized by a polymerase);

b) incubating said target polynucleotide with an RNA polymerase (with T7 or T3 RNA polymerase; see Figure 4), an initiator (or 1mM GMP; see page 3456, 2nd column, bottom paragraph) and a terminator (fluoresecent dye terminator; see page 3457, 1st column, bottom paragraph);

c) synthesizing oligonucleotide transcripts that is complementary to the initiation start site of the abortive promoter cassette, until dye terminator is incorporated in to the transcription product (see page 3457, Figure 4);

d) detecting the oligonucleotide transcripts by electrophoresis sequencing method (see Figure 5; page 3460, 1st column).

Kang et al. disclose a method of sequencing nucleic acid via use of RNA dependent RNA polymerases (column 9, lines 16-35 and 43-57), wherein the transcription of the template is initiated by a promoter sequence. An embodiment of the teachings of Kang et al. is drawn to the hybridization of the target nucleic acid to a primer which comprises a promoter sequence, wherein said primer is immobilized on a solid surface.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dattagupta and Sasaki et al., with the teachings of Kang et al., thereby arriving at the invention as claimed for the following reasons.

Dattagupta clearly provides that multiple transcripts can be derived from their method, wherein the multiple transcripts are provided by the use of a hairpin nucleic acid construct comprising a promoter sequence. While Sasaki et al. involve a different method for transcriptional sequencing, one of ordinary skill in the art would have clearly recognized that the method provided for by Dattagupta would have also been capable of conducting transcriptional sequencing by incorporating nucleotide chain terminators in their reaction.

One of ordinary skill in the art would have had a reasonable expectation of success at combining the teachings since both methods involve the generation of nucleic acid constructs comprising promoter sequences.

In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the teachings of Dattagupta and Sasaki et al. and Kang et al. for the purpose of detection/characterizing pathogens (such as RNA virus) in a sample, for the well known benefit of survival of mankind.

Such benefit is clearly implied by Sasaki et al., wherein the artisans explicitly state that their method would be useful in diagnostics, clinical diagnosis and genome sequencing. Clearly, one of ordinary skill in the art would have recognized that clinical diagnosis would undoubtedly include detection of pathogens in clinical samples. Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of Sasaki et al. with the teachings of Kang et al. so as to detect pathogens such as RNA-based pathogens. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at producing the combination since both teachings relied on the template nucleic acid having a promoter sequence which is recognized by the RNA dependent RNA polymerase to initiate the transcription reaction, wherein the transcription reaction is terminated by the incorporation of a terminating nucleotide.

Lastly, one of ordinary skill in the art at the time the invention was made would have recognized that any type of RNA polymerase would work equally well as Dattagupta clearly implies:

> "However, RNA probes transcribable with RNA-dependent RNA polymerases (such as in certain viruses, e.g., retrovirus and picornavirus)." (column 5, lines 23-24)

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

The rejection of claims 131 and 132 under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (U.S. Patent No. 5,215,899, issued June 1, 1993) in view of Sasaki et al.

(PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference) as applied to claims 55-70, 113, 130, 133-135, 138-140, 142-148 above, and further in view of Loewy (U.S. Patent No. 5,914,229, issued June 22, 1999, filed June 14, 1996), made in the Office Action mailed on December 11, 2007 is maintained for the reasons already of record.

Applicants do not make any new arguments for the present rejection in their Amendment received on June 11, 2008, but solely rely on their arguments presented for the above rejection. As the arguments have been fully rebutted as discussed above, the present rejection is maintained for the reasons already of record.

The Rejection:

The teachings of Dattagupta and Sasaki et al. have already been discussed above.

Neither of the artisans disclose a double stranded oligonucleotide construct which bind RNA polymerase.

Loewy discloses a double stranded nucleic acid promoter which bind RNA polymerase, employed in a method comprising:

a) providing a target nucleic acid as a single-stranded nucleic acid;

b) combining with said nucleic acid at least one oligonucleotide, where in the oligonucleotide or oligonucleotids include a double-stranded promoter, a single-stranded segment of nucleic acid complementary to a segment of the target nucleic acid, and a poly-T tail; and

c) contacting the oligonucleotide and the target nucleic acids; and

d) adding an RNA polymerase and ribonucleoside triphosphates or analogs thereof (column 4, lines 17-29)

It would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of Dattagupta and Sasaki et al., with the teachings of Loewy, thereby arriving at the claimed invention for the following reasons.

Dattagupta clearly disclose a method of hybridizing a promoter construct to a target nucleic acid, for the purpose of generating a multiple transcript products from the hybridized target nucleic acids. While the promoter construct hybridized employed by Dattagupta is drawn to a single, self-complementary nucleic acid comprising an overhang that hybridized to the target nucleic acid, one of ordinary skill in the art would have clearly recognized that the double-stranded promoter construct of Loewy would have also produced the same predictable result.

One of ordinary skill in the art would have had a reasonable expectation of success at combining the teachings as both Dattagupta and Loewy employed the hybridization of promoter construct to a target nucleic acid, for the purpose of generating multiple transcripts therefrom.

In *KSR Int'l Co. v. Teleflex Inc.,* (82 USPQ2d 1385, 127 SCt 1727, U.S. Supreme Court), the court expressed that there are, "[t]here cases decided after *Graham* [that] illustrate this doctrine…In *United States v. Adams,*…[t]he court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result."

The instant situation is analogous to that which was described by the court. One of ordinary skill in the art would have had concluded that substitution of one promoter construct for another promoter construct would have yield a predictable result.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

The rejection of claims 131 and 132 under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (U.S. Patent No. 5,215,899, issued June 1, 1993), Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460; IDS reference) and Kang et al. (U.S. Patent No. 6,268,131, issued July 31, 2001) as applied to claims 71, 113, 114, 130, 133, 135, 138-140, and 142-148 above, and further in view of Loewy (U.S. Patent No. 5,914,229, issued June 22, 1999, filed June 14, 1996), made in the Office Action mailed on December 11, 2007 is maintained for the reasons already of record.

Applicants' argument with respect to this rejection appears to be missing as Applicants only traverse and address only "three" obviousness rejections, where the office action contained a fourth, the present obviousness rejection.

However, it is assumed that Applicants' arguments would rely on the initial obviousness rejection over Dattagupta and Sasaki et al., the arguments of which have already been fully rebutted above.

Therefore, the rejection is maintained for the reasons already of record.

The Rejection:

The teachings of Dattagupta, Sasaki et al., and Kang et al. have already been discussed above.

None of these artisans disclose a double stranded oligonucleotide construct which bind RNA polymerase.

Loewy discloses a double stranded nucleic acid promoter which bind RNA polymerase, employed in a method comprising:

a) providing a target nucleic acid as a single-stranded nucleic acid;

b) combining with said nucleic acid at least one oligonucleotide, where in the oligonucleotide or oligonucleotids include a double-stranded promoter, a single-stranded

segment of nucleic acid complementary to a segment of the target nucleic acid, and a poly-T tail; and

c) contacting the oligonucleotide and the target nucleic acids; and

d) adding an RNA polymerase and ribonucleoside triphosphates or analogs thereof (column 4, lines 17-29)

It would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of Dattagupta, Sasaki et al., and Kang et al., with the teachings of Loewy, thereby arriving at the claimed invention for the following reasons.

Dattagupta clearly disclose a method of hybridizing a promoter construct to a target nucleic acid, for the purpose of generating a multiple transcript products from the hybridized target nucleic acids. While the promoter construct hybridized employed by Dattagupta is drawn to a single, self-complementary nucleic acid comprising an overhang that hybridized to the target nucleic acid, one of ordinary skill in the art would have clearly recognized that the double-stranded promoter construct of Loewy would have also produced the same predictable result.

One of ordinary skill in the art would have had a reasonable expectation of success at combining the teachings as both Dattagupta and Loewy employed the hybridization of promoter construct to a target nucleic acid, for the purpose of generating multiple transcripts therefrom.

In *KSR Int'l Co. v. Teleflex Inc.,* (82 USPQ2d 1385, 127 SCt 1727, U.S. Supreme Court), the court expressed that there are, "[t]here cases decided after *Graham* [that] illustrate this doctrine…In *United States v. Adams,*…[t]he court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one

element for another known in the field, the combination must do more than yield a predictable result."

The instant situation is analogous to that which was described by the court. One of ordinary skill in the art would have had concluded that substitution of one promoter construct for another promoter construct would have yield a predictable result.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Double Patenting

The provisional rejection of claims 55-71, 113, 114, 130-135, 138-140, and 142-148 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26, 27, 103, 112, and 136-139 of copending Application No. 10/488,971 (herein, the '971 application), made in the Office Action mailed on March 22, 2007 is withdrawn in view of a careful reconsideration of the application. The '971 application does not involve an abortive promoter construct as presently claimed, but rather rely on a binding of a target-site probe which, upon hybridization to the target nucleic acid, forms a bubble complex comprising a first double stranded region, a middle non-complementary region, and a second double stranded region. The two methods, thus involve patentably different constructs for the purpose of achieving their method, and thus the rejection is withdrawn.

The provisional rejection of claims 55-71, 113, 114, 130-135, 138-140, and 142-148 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-27 of copending Application No. 10/425,037, made in the Office Action mailed on March 22, 2007 is withdrawn in view of the finding that the '037 application has been abandoned on June 20, 2008.

Rejection, Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 55-71, 113, 114, 130-135, 138-140, and 142-148 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 32-34, and 44 of copending Application No. 10/976,240 (herein, the '240 application), made in the Office Action mailed on December 11, 2007 is maintained for the reasons already of record.

Applicants do not present any arguments for the instant rejection and thus, the rejection is maintained.

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Applicants' representative is encouraged to contact the Examiner of record for a possible negotiation of allowable subject matter.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
9/5/2008

/YJK/